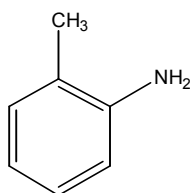


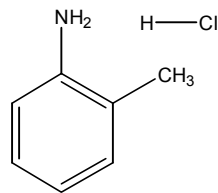
***o*-TOLUIDINE and *o*-TOLUIDINE HYDROCHLORIDE**

CAS Nos. 95-53-4 and 636-21-5

First Listed in the *Third* and *Second Annual Reports on Carcinogens*, respectively



o-Toluidine



o-Toluidine hydrochloride

CARCINOGENICITY

o-Toluidine and *o*-toluidine hydrochloride are *reasonably anticipated to be human carcinogens* based on sufficient evidence for the carcinogenicity of *o*-toluidine hydrochloride in experimental animals (IARC V.16, 1978; IARC V.27, 1982; IARC S.4, 1982; IARC S.7, 1987). When administered in the diet, *o*-toluidine hydrochloride increased the incidences of hepatocellular carcinomas or adenomas in female mice and hemangiosarcomas at multiple sites in male mice of one strain and hemangiosarcomas and hemangiomas of the abdominal viscera in both sexes of another strain. When administered in the diet, *o*-toluidine hydrochloride increased the incidences of sarcomas of multiple organs in rats of both sexes, subcutaneous fibromas and mesotheliomas in male rats, and sarcomas of the spleen, transitional cell papillomas and carcinomas of the urinary bladder, and mammary gland fibroadenomas and adenomas in female rats. In male rats of another strain, the compound increased the incidences of subcutaneous fibromas and fibrosarcomas; a few transitional cell carcinomas of the urinary bladder were also seen. There are no evaluable studies of the carcinogenicity of the free base, *o*-toluidine, in experimental animals.

There is inadequate evidence for the carcinogenicity of *o*-toluidine and *o*-toluidine hydrochloride in humans. (IARC S.7, 1987). Although an excess of bladder tumors has often been found in workers exposed to varying combinations of dyestuffs and dyestuff intermediates, no population of workers exposed to *o*-toluidine alone has been described. Occasional cases of bladder tumors have been reported in workers classified as being exposed primarily to *o*-toluidine, but either insufficient data or insufficient follow-up time have prevented a clear association being made with the exposure. An excess of bladder tumors was noted in workers exposed to toluene, *o*-nitrotoluene, *o*-toluidine, and 4,4N-methylenebis(2-methylaniline) during the manufacture of new fuchsin and safranine (IARC S.7, 1987).

PROPERTIES

o-Toluidine is a liquid that is slightly soluble in water, miscible with carbon tetrachloride, diethyl ether, and ethanol. When heated, it emits toxic fumes of nitrogen oxides (NO_x) and can react with oxidizing materials. *o*-Toluidine hydrochloride is a powder that is very soluble in water and ethanol but insoluble in benzene and diethyl ether. When heated to decomposition, it emits toxic fumes of hydrochloric acid (HCl) and nitrogen oxides (NO_x). *o*-Toluidine is available in the United States as a technical grade with a minimum of 99.5% purity, containing *m*- and *p*-toluidine as impurities. The commercial product may also contain a stabilizer.

USE

o-Toluidine and *o*-toluidine hydrochloride are used primarily as intermediates in the manufacture of a variety of dyes, including azo pigment dyes, triarylmethane dyes, sulfur dyes, and indigo compounds. The Society of Dyers and Colourists reported that 93 dyes and pigments can be prepared from these compounds and their derivatives, of which 16 were produced commercially in the United States in 1979. These dyes are used primarily for printing textiles, as biological stains, and in color photography. *o*-Toluidine is also used as an intermediate for rubber vulcanizing chemicals, pharmaceuticals, and pesticides. Other minor uses of *o*-toluidine are as an intermediate in chemical production and as an ingredient in clinical laboratory reagents for determining glucose and hemoglobin (IARC, V.27, 1982).

PRODUCTION

Chem Sources identified two suppliers of analytical grade *o*-toluidine among the twenty-two listed, and ten suppliers of *o*-toluidine hydrochloride in 1990 (Chem Sources, 1991). The USITC has identified two U.S. producers of *o*-toluidine since 1988, but no production volumes were provided (USITC, 1990; USITC, 1989). In 1986, there were three producers of *o*-toluidine and one producer of *o*-toluidine hydrochloride (SRIa, 1986). No production volumes are available for *o*-toluidine hydrochloride; however, the Chem Sources USA directory identified 12 suppliers in 1986 (Chem Sources, 1986). In 1983, U.S. production of *o*-toluidine was between 11 million and 21 million lb; the Chem Sources USA directory identified 34 companies as suppliers of *o*-toluidine in 1983 (Chem Sources, 1983). The United States imported 35,700 lb of *o*-toluidine and 992 lb of its hydrochloride in 1983 (EPA ETD, 1984).

The 1979 TSCA Inventory identified two companies producing 500 lb of *o*-toluidine hydrochloride in 1977 and one importer, with no volume reported. The CBI Aggregate was less than 1 million lb (TSCA, 1979). Commercial production was first reported in the United States in 1922 for *o*-toluidine and in 1956 for *o*-toluidine hydrochloride (IARC V.27, 1982).

EXPOSURE

The primary routes of potential human exposure to *o*-toluidine and *o*-toluidine hydrochloride are inhalation, ingestion, and dermal contact. OSHA reported that an estimated 13,900 workers were possibly exposed to *o*-toluidine. The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 13,053 workers were potentially exposed to *o*-toluidine in the workplace (NIOSH, 1976). The National Occupational Exposure Survey (1981-1983) indicated that 5,440 workers, including 2,561 women, potentially were exposed to *o*-toluidine and 154 total workers potentially were exposed to *o*-toluidine hydrochloride (NIOSH, 1984). Occupations with the greatest potential for exposure to the compounds include dyemakers and pigment makers. *o*-Toluidine residues are present in products used as acid inhibitors at concentrations of < 0.5%. *o*-Toluidine concentration; in the air at a plant producing dyes and pigments was measured to be between 0.004 and 0.26 ppm. In area samples taken in the air of two coal liquification pilot facilities, the mean concentration of *o*-toluidine was < 0.1 ppm. Although medical and laboratory personnel represent a significant population of workers potentially exposed to *o*-toluidine, air concentrations have been determined to be below 22 µg/l (CHIP, 1984b). The ACGIH recommended threshold limit value (TLV) for *o*-toluidine is # 2 ppm (9 mg/m³) as an 8-hr time-weighted average (TWA), with a

skin notation (ACGIH, 1986). Consumer exposure to *o*-toluidine may possibly occur from residues present in commercial dyes used on textiles. Also, *o*-toluidine is reported to be present in cigarette smoke at the rate of 32 ng/cigarette (OSH, 1982). The presence of *o*-toluidine, even as a trace contaminant, would be a cause for concern. *o*-Toluidine has been detected in the effluents from refineries and production facilities, in river water, process water, and ground water (CHIP, 1984b). The Toxic Chemical Release Inventory (EPA) listed 21 industrial facilities that produced, processed, or otherwise used *o*-toluidine in 1996 (TRI, 1999). In compliance with the Community Right-to-Know Program the facilities reported releases of *o*-toluidine to the environment which were estimated to total 35301 lb.

REGULATIONS

In 1980 CPSC preliminarily determined that *o*-toluidine and *o*-toluidine hydrochloride were not present in consumer products under its jurisdiction. Subsequently, public comment was solicited to verify the accuracy of this information; no comments were received. Pending receipt of new information, CPSC plans no action on this chemical. EPA regulates *o*-toluidine and *o*-toluidine hydrochloride under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), Superfund Amendments and Reauthorization Act (SARA), and Toxic Substances Control Act (TSCA). A reportable quantity (RQ) of 100 lb has been established for *o*-toluidine and *o*-toluidine hydrochloride under CERCLA. Under RCRA, EPA regulates *o*-toluidine hydrochloride as a hazardous constituent of waste, and has proposed regulating wastes containing *o*-toluidine. SARA placed both *o*-toluidine and the *o*-toluidine hydrochloride on a list of toxic chemicals subject to reporting requirements. TSCA requires reporting of health and safety studies by manufacturers of *o*-toluidine. FDA reports that exposure to *o*-toluidine is limited to trace amounts in any products under its jurisdiction; therefore, it has not taken regulatory action against the compounds. OSHA adopted a permissible exposure limit (PEL) of 5 ppm (22 mg/m³) as an 8-hr time-weighted average (TWA) for occupational exposure to *o*-toluidine based on toxic effects other than cancer. OSHA also regulates *o*-toluidine and *o*-toluidine hydrochloride under the Hazard Communication Standard and chemical hazards in laboratories. Regulations are summarized in Volume II, Table B-143.